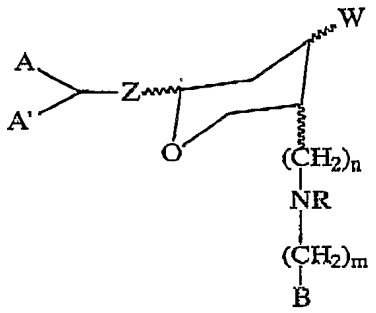
AMENDED CLAIMS

[received by the International Bureau on 10 October 2005 (10.10.2005);
original claims, 16 and 17 amended; new claims 25-29 added;
remaining claims unchanged (16 pages)]

1. A 3,6-substituted pyran group-containing compound having the structural formula:



wherein

A, A′, and B are individually selected from the group of optionally substituted C_4-C_{14} aryl and heteroaryl wherein heteroatoms of heteroaryl A and/or A′ are selected from the group consisting of O, N, and S;

Z is selected from the group consisting of a chemical bond and -Y-$(CH_2)_o$- wherein Y is NH or O and o is 0, 1, 2, 3, or 4;

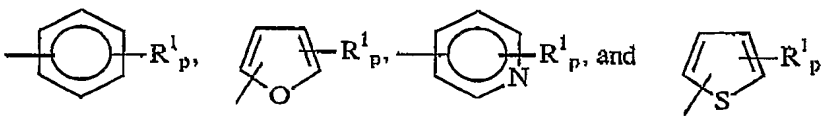
R is H or C_{1-8} alkyl;

W is selected from the group consisting of hydrogen and -OH; and

n and m individually are 0, 1, 2, 3, or 4, and wherein any carbon of -$(CH_2)_n$ may be substituted by OR^4 wherein R^4 is C_{1-8} alkyl, C_{2-18} alkylene, or -$COOR^5$ wherein R^5 is C_{1-18} alkyl or C_{2-18} alkylene, and when W is H, B is an optionally substituted indolyl group, a 4-hydroxybenzyl group, an iodophenyl group, or a 4-aminobenzyl group,

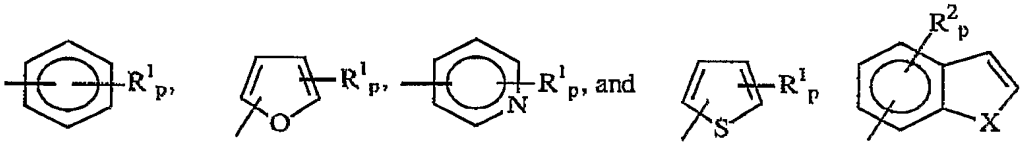
or a pharmaceutically acceptable derivative or salt thereof.

2. The compound of claim 1, wherein at least one of A and A′ are selected from the group consisting of:



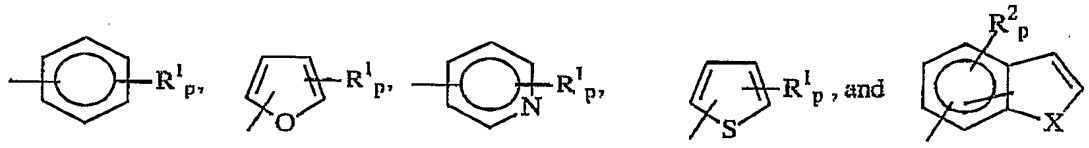
where R^1 is selected from the group consisting of C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} optionally halogenated alkynyl, C_{2-6} hydroxyalkynyl, halo, -CN, -COOR, where R is C_{1-18} alkyl, C_{5-10} cycloalkyl, C_{2-18} alkenyl, -OH, $-NO_2$, $-NH_2$, $-OR^2$ where R^2 is C_{1-8} alkyl, C_{5-6} cycloalkyl, or C_{2-8} alkenyl.

3. The compound of claim 1, wherein B is selected from the group



where R^1 is selected from the group consisting of C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} optionally halogenated alkynyl, C_{2-6} hydroxyalkynyl, halo, -CN, -COOR, where R is C_{1-18} alkyl, C_{5-10} cycloalkyl, C_{2-18} alkenyl, -OH, $-NO_2$, $-NH_2$, $-OR^2$ where R^2 is C_{1-8} alkyl, C_{5-6} cycloalkyl, or C_{2-8} alkenyl; and
wherein R^2 have the meaning of R^1 and also a 5 or 6 membered heterocycle containing 1 or more heteroatoms selected from the group consisting of N, O, and S, and wherein X is N, O, or S.

4. The compound of claim 2, wherein B is selected from the group



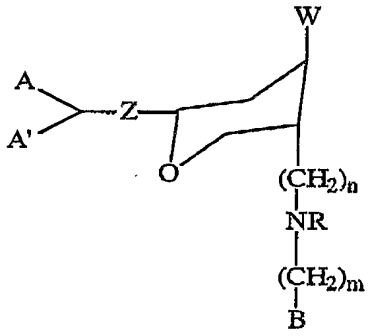
where R^1 is selected from the group consisting of C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} optionally halogenated alkynyl, C_{2-6} hydroxyalkynyl, halo, -CN, -COOR, where R

is C_{1-18} alkyl, C_{5-10} cycloalkyl, C_{2-18} alkenyl, -OH, $-NO_2$, $-NH_2$, $-OR^2$ where R^2 is C_{1-8} alkyl, C_{5-6} cycloalkyl, or C_{2-8} alkenyl; and

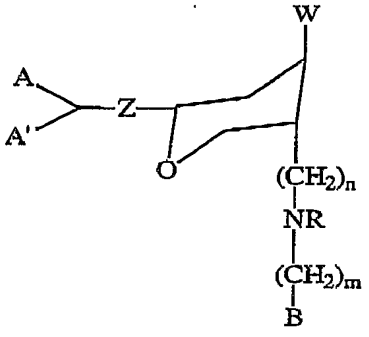
wherein R^2 have the meaning of R^1 and also a 5 or 6 membered heterocycle containing 1 or more heteroatoms selected from the group consisting of N, O, and S, and wherein X is N, O, or S.

5. The compound of claim 3, wherein A and A′ are both unsubstituted phenyl.

6. The compound of claim 1, having the formula

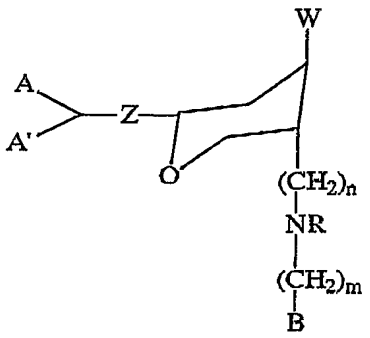


7. The compound of claim 2, having the formula



AMENDED SHEET (ARTICLE 19)

1 8. The compound of claim 3, having the formula



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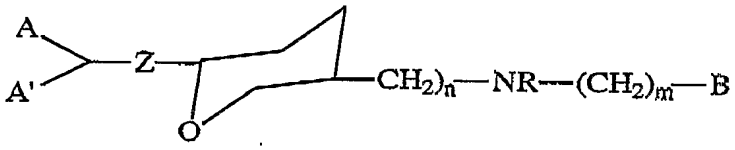
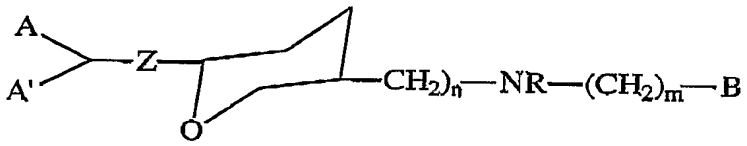
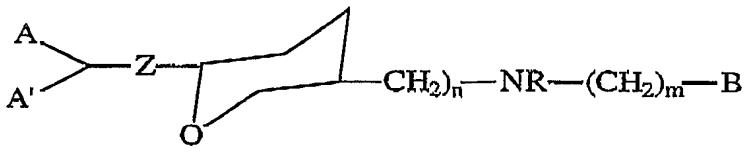
1 9. The compound of claim 1, having the formula



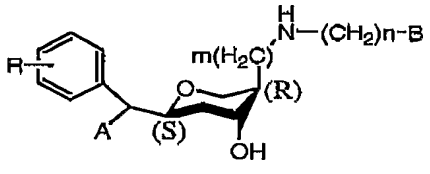
1 10. The compound of claim 2, having the formula



11. The compound of claim 3, having the formula



12. The compound of claim 1, having a formula selected from the group consisting of:



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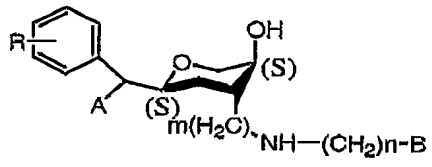

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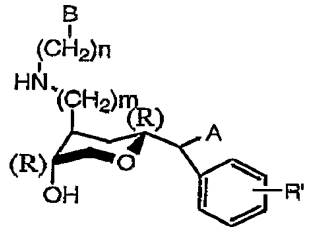

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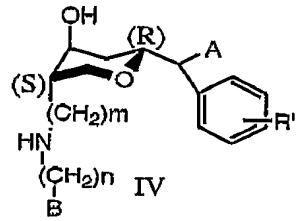

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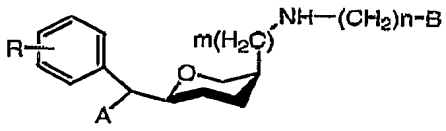
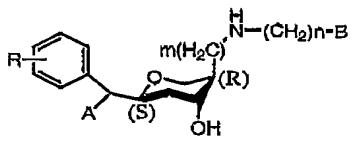


V

13. The compound of claim 2, having a formula selected from the group consisting of:



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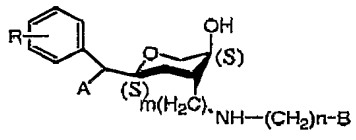

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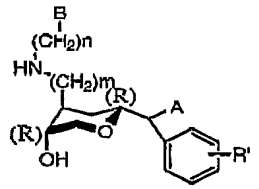

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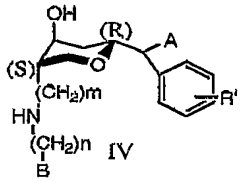

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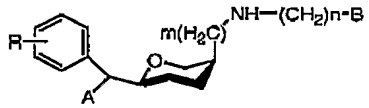

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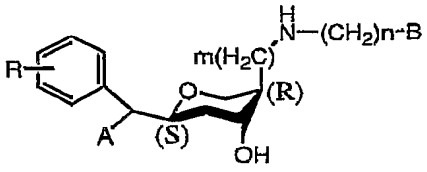
14. The compound of claim 3, having a formula selected from the group consisting of:



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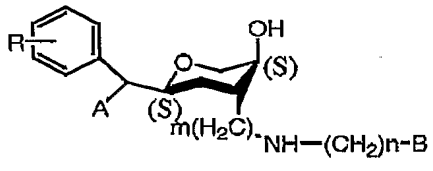

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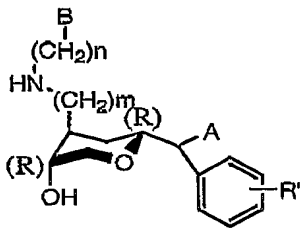

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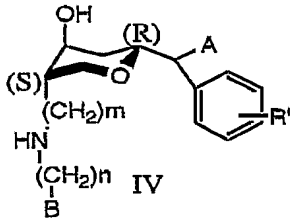

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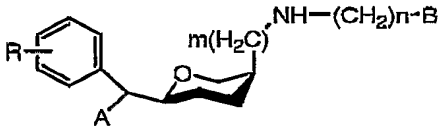

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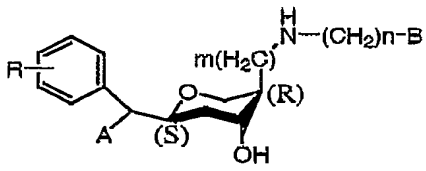
15. The compound of claim 5, having a formula selected from the group consisting of:



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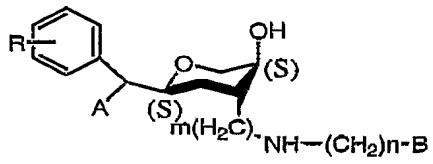

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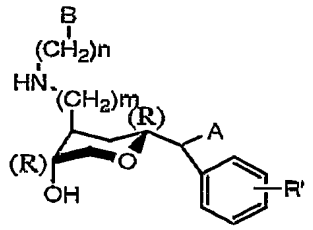

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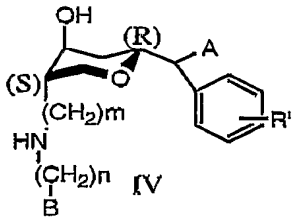

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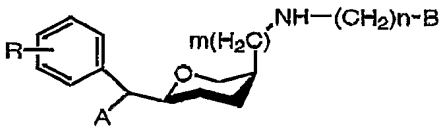


V

16. The compound of claim 1, selected from the group consisting of:

cis-(6-benzhydryl-tetrahydropyran-3-yl)-(4-hydroxy-benzyl)-amine;

cis-(6-benzhydryl-tetrahydropyran-3-yl)-(1H-iodo-5-ylmethyl)-amine;

cis-(6-benzhydryl-tetrahydropyran-3-yl)-(4-amino-benzyl)-amine;

cis-(6-benzhydryl-tetrahydropyran-3-yl)-(3,4-dichloro-benzyl)-amine;

(2S, 4R, 5R)-2-benzhydryl-5-(4-methoxy-benzylamino)-tetrahydropyran-4-ol;

(2S, 4R, 5R)-2-benzhydryl-5-(4-fluoro-benzylamino)-tetrahydro-pyran-4-ol;

(2S, 4R, 5R)-2-benzhydryl-5-benzylamino-tetrahydro-pyran-4-ol;

(2S, 4R, 5R)-2-benzhydryl-5-(2,4-dimethoxy-benzylamino)-tetrahydropyran-4-ol;

(2S, 4R, 5R)-2-benzhydryl-5-(3,5-dimethoxy-benzylamino)-tetrahydropyran-4-ol;

(2S, 4R, 5R)-2-benzhydryl-5-(4-hydroxy-benzylamino)-tetrahydropyran-4-ol;

(2S, 4R, 5R)-2-benzhydryl-5-[(1H-indol-5-ylmethyl)-amino]-tetrahydropyran-4-ol;

(2R, 4S, 5S)-2-benzhydryl-5-(4-hydroxy-benzylamino)-tetrahydro-pyran-4-ol;

(2R, 4S, 5S)-2-benzhydryl-5-[(1H-indol-5-ylmethyl)-amino]-tetrahydropyran-4-ol;

cis-(3S, 6S)-(6-benzhydryl-tetrahydropyran-3-yl)-(4-hydroxy-benzyl)-amine; and

cis-(3R, 6R)-(6-benzhydryl-tetrahydropyran-3-yl)-(4-hydroxy-benzyl)-amine.

17. The compound of claim 1, selected from the group consisting of:

(2S, 4R, 5R)-2-benzhydryl-5-(4-methoxy-benzylamino)-tetrahydropyran-4-ol;

(2S, 4R, 5R)-2-benzhydryl-5-(4-fluoro-benzylamino)-tetrahydro-pyran-4-ol;

(2S, 4R, 5R)-2-benzhydryl-5-benzylamino-tetrahydro-pyran-4-ol;

(2S, 4R, 5R)-2-benzhydryl-5-(2,4-dimethoxy-benzylamino)-tetrahydropyran-4-ol;

(2S, 4R, 5R)-2-benzhydryl-5-(3,5-dimethoxy-benzylamino)-tetrahydropyran-4-ol;

(2S, 4R, 5R)-2-benzhydryl-5-(4-hydroxy-benzylamino)-tetrahydropyran-4-ol;

(2S, 4R, 5R)-2-benzhydryl-5-[(1H-indol-5-ylmethyl)-amino]-tetrahydropyran-4-ol;

(2R, 4S, 5S)-2-benzhydryl-5-(4-hydroxy-benzylamino)-tetrahydro-pyran-4-ol;

AMENDED SHEET (ARTICLE 19)

(2R, 4S, 5S)-2-benzhydryl-5-[(1H-indol-5-ylmethyl)-amino]-tetrahydropyran-4-ol;

cis-(3S, 6S)-(6-benzhydryl-tetrahydropyran-3-yl)-(4-hydroxy-benzyl)-amine; and

cis-(3R, 6R)-(6-benzhydryl-tetrahydropyran-3-yl)-(4-hydroxy-benzyl)-amine.

18. A method of reducing monoamine reuptake in a mammalian species, comprising administering a binding amount of a monoamine receptor binder comprising a compound of claim 1.

19. A method of reducing monoamine reuptake in a mammalian species, comprising administering a binding amount of a monoamine receptor binder comprising a compound of claim 2.

20. A method of reducing monoamine reuptake in a mammalian species, comprising administering a binding amount of a monoamine receptor binder comprising a compound of claim 12.

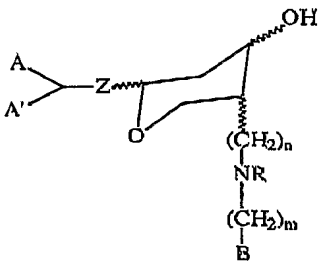
21. A method for the treatment of depression, comprising administering to a patient exhibiting signs of depression, a compound of claim 1 in an amount effective to inhibit reuptake of serotonin at the SERT and norepinephrine at the NET.

22. The method of claim 21 wherein the compound exhibits greater inhibition of serotonin and norepinephrine reuptake than of dopamine reuptake.

23. A method for the treatment of depression, comprising administering to a patient exhibiting signs of depression, a compound of claim 1 in an amount effective to inhibit norepinephrine reuptake at the NET.

24. The method of claim 23 wherein said compound exhibits higher norepinephrine reuptake inhibition than serotonin reuptake inhibition and dopamine reuptake inhibition.

25. 1. A 3,6-substituted pyran group-containing compound having the structural formula:



wherein

A, A′, and B are individually selected from the group of optionally substituted C_4-C_{14} aryl and heteroaryl wherein heteroatoms of heteroaryl A and/or A′ are selected from the group consisting of O, N, and S;

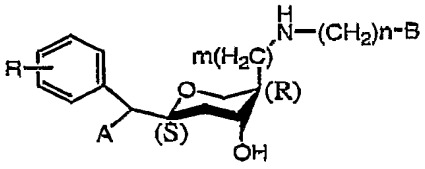
Z is selected from the group consisting of a chemical bond and -Y-$(CH_2)_o$- wherein Y is NH or O and o is 0, 1, 2, 3, or 4;

R is H or C_{1-8} alkyl;

n and m individually are 0, 1, 2, 3, or 4, and wherein any carbon of -$(CH_2)_n$ may be substituted by OR^4 wherein R^4 is C_{1-8} alkyl, C_{2-18} alkylene, or -$COOR^5$ wherein R^5 is C_{1-18} alkyl or C_{2-18} alkylene,

or a pharmaceutically acceptable derivative or salt thereof.

26. The compound of claim 25, having a formula selected from the group consisting of:



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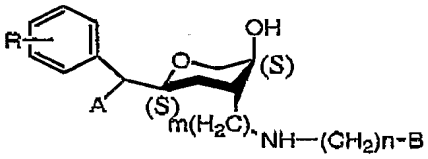

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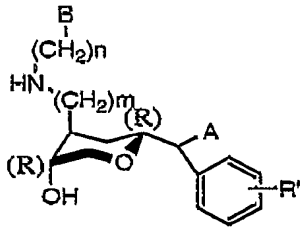

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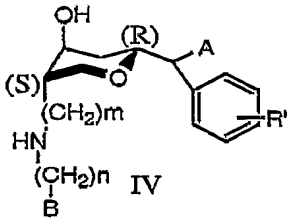

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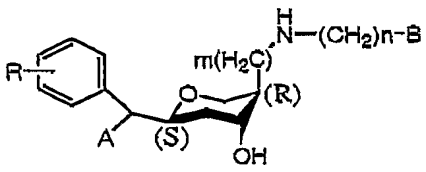
27. The compound of claim 25, having a formula selected from the group consisting of:



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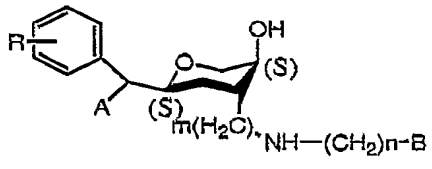

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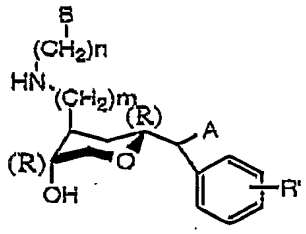

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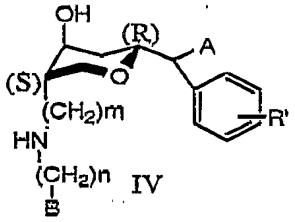
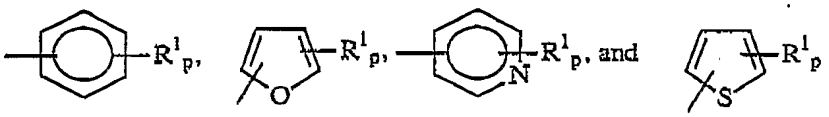


IV

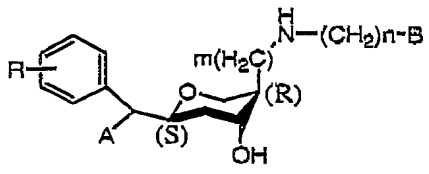
wherein A is selected from the group consisting of:



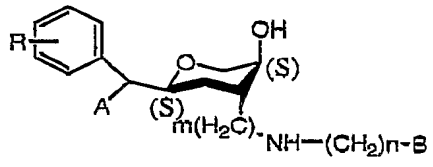
where R^1 is selected from the group consisting of C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} optionally halogenated alkynyl, C_{2-6} hydroxyalkynyl, halo, -CN, -COOR, where R is C_{1-18} alkyl, C_{5-10} cycloalkyl, C_{2-18} alkenyl, -OH, $-NO_2$, $-NH_2$, $-OR^2$ where R^2 is C_{1-8} alkyl, C_{5-6} cycloalkyl, or C_{2-8} alkenyl.

AMENDED SHEET (ARTICLE 19)

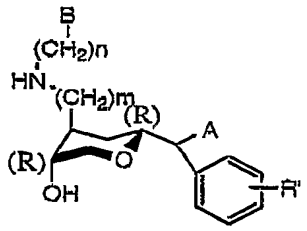
28. The compound of claim 25,, having a formula selected from the group consisting of:



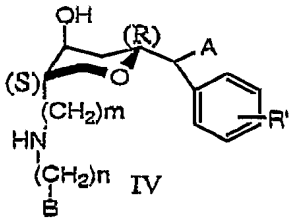
I



II

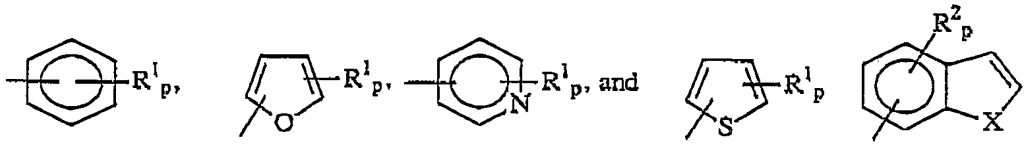


III



IV

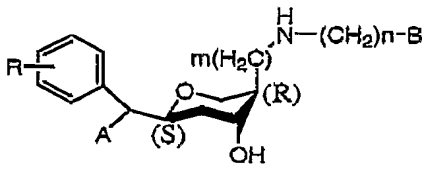
wherein B is selected from the group



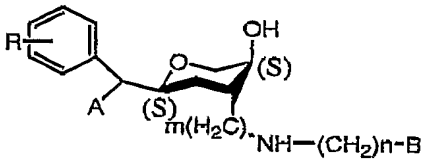
where R^1 is selected from the group consisting of C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} optionally halogenated alkynyl, C_{2-6} hydroxyalkynyl, halo, -CN, -COOR, where R is C_{1-18} alkyl, C_{5-10} cycloalkyl, C_{2-18} alkenyl, -OH, $-NO_2$, $-NH_2$, $-OR^2$ where R^2 is C_{1-8} alkyl, C_{5-6} cycloalkyl, or C_{2-8} alkenyl; and

wherein R^2 have the meaning of R^1 and also a 5 or 6 membered heterocycle containing 1 or more heteroatoms selected from the group consisting of N, O, and S, and wherein X is N, O, or S.

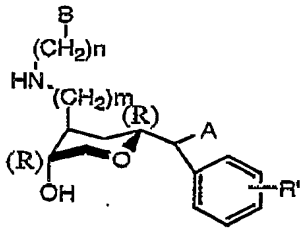
29. The compound of claim 27, having a formula selected form the group consisting of:



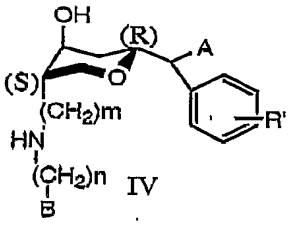
I



II

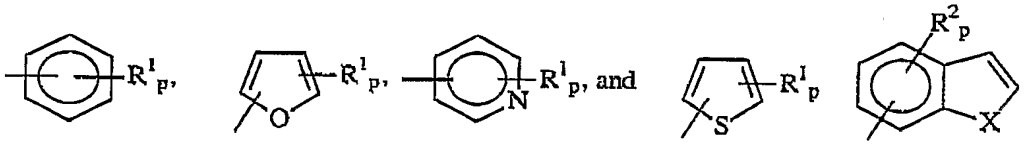


III



IV

wherein B is selected from the group



where R^1 is selected from the group consisting of C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} optionally halogenated alkynyl, C_{2-6} hydroxyalkynyl, halo, -CN, -COOR, where R

is C_{1-18} alkyl, C_{5-10} cycloalkyl, C_{2-18} alkenyl, -OH, -NO_2, -NH_2, -OR^2 where R^2 is C_{1-8} alkyl, C_{5-6} cycloalkyl, or C_{2-8} alkenyl; and

wherein R^2 have the meaning of R^1 and also a 5 or 6 membered heterocycle containing 1 or more heteroatoms selected from the group consisting of N, O, and S, and wherein X is N, O, or S.